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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,059	08/02/2004	Bernd Stahl	STAH3007/REF	4218

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,059	STAHL ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32 and 35* is/are rejected.

7)☒ Claim(s) *23 and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page/02Aug04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is the 371 national stage entry of PCT/EP03/00505, filed 20 January 2003, claiming benefit of foreign priority document Germany 102 03 999.2, filed 1 February 2002. Claims 19-35 are pending in the instant application. Claims 33 and 34, drawn to a nonelected invention, are withdrawn. Claims 19-32 and 35 are examined on the merits herein.

Election/Restrictions

Applicant's election without traverse of the invention of Group I, claims 19-32 and 35, in the reply filed on 23 August 2007 is acknowledged.

Claims 34 and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 23 August 2007.

Applicant's election with traverse of the species cyclogycan in the reply filed on 23 August 2007 is acknowledged. The traversal is on the ground(s) that a method of treatment with the cycloglycan bound to an inert carrier should be considered the same invention as a method of treatment with the cycloglycan itself. This is found persuasive because applicant argues it is a common pharmaceutical feature to anchor or bind a pharmacological active substance to an inert carrier. Therefore, the species election requirement is withdrawn.

The restriction requirement to the invention of Group I is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement filed 2 August 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. In order to facilitate prosecution of the application and due to the small number of references not provided, the information will be considered.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a

nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The disclosure is objected to because of the following informalities:

The instant application contains only one section titled, "DESCRIPTION". It is unclear whether section of the specification this corresponds to, and

The presence of minor spelling and grammatical errors, such as:

Page 2, line 15, "acuiring" is misspelled.

Page 3, line 17, "cycloglycanes" is misspelled.

Page 7, line 19, "procaryontic" and "eucaryontic" are both misspelled.

Page 8, line 17-18, "Listeria monocytogenes" is the name of a species and should appear in italics.

Page 8, line 24, "infectuous" is misspelled.

Page 9, line 4, "infectuous" is misspelled.

Page 9, line 7, "useded" is misspelled.

Page 9, line 13, "aglukone" is misspelled.

Page 9, line 31, "babyfood" should be two words.

Appropriate correction is required.

Claim Objections

Claim 23 is objected to because of the following informalities: β-glycosidic is misspelled "β-iglycosidic". Appropriate correction is required.

Claim 29 is objected to because of the following informalities: Claim 29 as disclosed depends from itself, "29. The method according to claim 29, ...". For the purposes of examination claim 29 has been interpreted by Examiner to mean "the method according to claim 28," based on the reference to a composition. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing or preventing the invasion and infection of mammalian cells by pathogens and for combating diseases caused by such pathogens comprising administering to a mammal an effective amount of cycloglycans for some pathogens, diseases, and cycloglycans, does not reasonably provide enablement for all pathogens, diseases, and cycloglycans or for preventing the invasion and infection of mammalian cells by pathogens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a

disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: A method for reducing or preventing the invasion and infection of mammalian cells by pathogens, and for combating diseases caused by such pathogens comprising administering to a mammal an effective amount of cycloglycans.

The state of the prior art: There is no prior art that teaches the prevention of invasion and infection of mammalian cells. Prevention is defined as "to keep from happening or arising, or to make impossible." See definition of prevent (WordNet, cited in PTO-892). It is not practicable to make invasion and infection of mammalian cells by pathogens impossible.

It is known that some cycloglycans may reduce the invasion and infection of mammalian cells by some pathogens. For example, methyl β-cyclodextrin may be used to inhibit infection by the virus, HIV, and the bacterium, *E. coli*. See Duncan et al., page 787, left column, lines 20-23 and right column, lines 45-49 (Cellular Microbiology, 2002, 4, p783-791, cited in PTO-892). However, Duncan et al. notes that methyl β-cyclodextrin does not inhibit invasion by opsonin mediated bacteria.

Jutras et al. discloses the use of methyl β-cyclodextrin to prevent invasion of HeLa cells by bacteria of the genus *Chlamyidia*. However, internalization of *E. coli*

expressing an invasin protein was not significantly impaired by treatment with methyl β-cyclodextrin. See Jutras et al., page 263, left column, lines 29-34 and 52-56 and right column, lines 1-4 (Infection and Immunity, 2003, 71, p260-266, cited in PTO-892).

Roth et al. discloses the use of β-cyclodextrin and derivatives to block HIV-1 entry. Roth et al. disclose the inhibition of infectivity for methyl β-cyclodextrin and β-cyclodextrin with 14 sulfate groups, but no inhibition for propyl β-cyclodextrin or β-cyclodextrin with 4 sulfate groups. See Roth et al., page 25, table 2 (WIPO publication WO/90/00596, provided by Applicant on IDS filed 2 August 2004).

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: As disclosed in the prior art, there is little predictability for which cyclogycans reduce the invasion and infection of mammalian cells by which pathogens. This unpredictability, combined with the sheer number of pathogens, diseases, and cycloglycans means that one skilled in the art cannot predict the usefulness for all possible methods of treatment. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims is infinite. Almost any possible chemical structure could potentially be used as the cyclogycan derivative as disclosed in claim 22 because, for example, no limitation is placed on the term ether, ester, amide, alkyl group. No limitation is placed on what pathogens or disease the treatment is meant to reduce, prevent, or combat.

The amount of direction or guidance presented: The specification speaks generally about cycloglycans that reduce or prevent the invasion and infection of

mammalian cells, such as listeria. See specification, page 8, lines 9-14. It is suggested that "results of the tests conducted clearly show that neither the process of phagocytosis as such, nor the replication of the ingested listeria is inhibited," meaing phagocytosis and replication of listeria is not inhibited, and therefore the method of reducing infection and invasion of cells by that pathogen is not enabled. However, guidance is not given for what "the tests" were, or for what cycloglycans may be used to reduce or prevent the invasion and infection of mammalian cells from what pathogens.

The presence or absence of working examples: No working examples are disclosed.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable art such as reducing or preventing the invasion and infection of mammalian cells by pathogens and combating diseases caused by such pathogens. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with the full range of all possible methods of reducing or preventing the invasion and infection of mammalian cells by pathogens and combating diseases caused by such pathogens comprising administering to a mammal an effective amount of cycloglycans beyond those known in the art, (such as methyl β-cyclodextrin administered to reduce HIV-1 infectivity) one skilled in the art would undertake a novel and extensive research program into the effectiveness of each cycloglycan in treating each pathogen or disease. Because this research would have to be exhaustive, and because it would

involve such a wide and unpredictable scope of pathogens, diseases, and cycloglycans, it would constitute an undue and unpredictable experimental burden.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention for all possible methods of reducing or preventing the invasion and infection of mammalian cells by pathogens and combating diseases caused by such pathogens comprising administering to a mammal an effective amount of cycloglycans.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-32 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Anand et al. (US Patent 5,221,669, provided by Applicant on IDS filed 2 August 2004).

Anand et al. discloses the α-cyclodextrin (CD) sulfate used to treat a viral infection, particularly HIV-1 or HIV-2, by administering α-cyclodextrin sulfate to a patient. See Anand et al., column 3, lines 1-21. HIV is an pathogenic virus that infects the blood system. Anand et al. discloses practicing the invention using other

cyclodextrin derivatives, for example hydroxypropyl α-CD sulfate and hydroxypropyl β-CD sulfate. See Anand et al., column 5, lines 6-8. Cyclodextrin is a cycloglucan composed of 6 (α-CD), 7 (β-CD), or 8 (γ-CD) glucose units linked by α(1-4) glycosidic bonds. See definition of cyclodextrin (The Merck Index, cited in PTO-892). Anand et al. discloses the α-CD sulfate in a pharmaceutical composition, for example in the form of an oral preparation including binders such as cellulose, starch, and gelatin. See column 10, lines 18-29. Anand et al. discloses, "the actual dose and schedule for drug administration for each patient will vary depending upon interindividual differences in pharmacokinetics, drug disposition and metabolism. Moreover, the dose may vary when the compounds are used prophylactically or when used in combination with other drugs. Such dosage amounts can be readily ascertained without undue burden and experimentation by those skilled in the art. As an example of an antiviral effective amount, the parenteral dosage for humans can range from about between 0.01 mg/kg body weight to 1200 mg/kg body weight." See Anand et al., column 11 lines 36-48 and column 12, lines 1-2. Given this disclosure, one of skill in the art would immediately envision, for example, a dosage of 1200 mg/kg body weight administered once daily.

Claims 19-25, 31, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Roth et al. (WIPO publication WO/90/00596, provided by Applicant on IDS filed 2 August 2004).

Roth et al. discloses using a carbohydrate to block cell to cell transmission of a virus, HIV. See Roth et al., page 9, lines 15-19. Roth et al. discloses the use of α-, β-,

and γ-CD, possibly derivatized at the C-2, 3, and 6 OH groups of the constituent sugars of the CD. See page 10, lines 7-10 and 17-19. Cyclodextrin is a cycloglucan composed of 6 (α-CD), 7 (β-CD), or 8 (γ-CD) glucose units linked by α(1-4) glycosidic bonds. See definition of cyclodextrin (The Merck Index, cited in PTO-892). Roth et al. discloses the specific CDs of β-CD, β-CD with 4 sulfate groups, β-CD with 4 propoxy groups, and β-CD with 14 sulfate groups. See Roth et al., page 24, lines 24-29. Roth et al. discloses the administration of the carbohydrate to cells within the body of a mammal by several routes of administration, for example the oral route. See Roth et al, page 15, lines 15-21.

Claims 19-29 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanchez et al. (US Patent 5,296,472, provided by Applicant on IDS filed 2 August 2004).

Sanchez et al. discloses the administration of γ-CD to ear canals to prevent skin and ear infections, the ear being part of the nasopharynx system. See Sanchez et al., column 10, lines 29-43. Cyclodextrin is a cycloglucan composed of 6 (α-CD), 7 (β-CD), or 8 (γ-CD) glucose units linked by α(1-4) glycosidic bonds. See definition of cyclodextrin (The Merck Index, cited in PTO-892). Sanchez et al. also discloses the use of hydroxyproyl β-CD and hydroxyproyl γ-CD. See Sanchez et al., column 2, lines 49-50. Sanchez et al. discloses formulations that include the CD bound to carriers such as oils, waxes, and lipid-type agents. See Sanchez, et al., column 5, lines 12-21.

Claims 19-29, 31, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Nelson (US Patent 6,261,540, provided by Applicant on IDS filed 2 August 2004).

Nelson discloses a method of treating oral infections with an oral composition. See Nelson, column 3, lines 46-49. Nelson discloses that the invention is for the treatment of bacterial infections in the mouth. See Nelson, column 1, lines 52-54. The mouth is a respiratory passage. Nelson discloses that the composition comprises hydroxyproyl β-CD or hydroxyproyl γ-CD. See Nelson, column 5, lines 11-20. Cyclodextrin is a cycloglucan composed of 6 (α-CD), 7 (β-CD), or 8 (γ-CD) glucose units linked by α(1-4) glycosidic bonds. See definition of cyclodextrin (The Merck Index, cited in PTO-892). Nelson discloses the oral pharmaceutical composition of a dental rinse with a carrier or binder, for example cellulose. See Nelson, column 7, lines 16-19 and 44-48.

Claims 19-25, 27-30, 32 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Bernstein (US Patent 4,020,160, cited in PTO-892).

Bernstein discloses the use of cyclodextrin sulfate salts, α-CD polysulfate, β-CD polysulfate, and γ-CD polysulfate, (column 3, lines 1-8) used to treat inflammatory states induced by bacterial enzymes (column 4, lines 1-3). This use is to combat a disease caused by bacterial pathogens. Bernstein discloses the CD used as a composition such as an oral composition, for example with the carrier corn starch, for oral administration, or for intra-articular administration. See Bernstein, column 7, lines 27-

29, 53-57, and 64. Bernstein discloses the CD administered at a dose of 5-50 mg/kg/day. See Bernstein, column 7, line 39.

Claims 19-21, 23-25, 28-31, and 35 are are rejected under 35 U.S.C. 102(b) as being anticipated by Castro Hermida et al. (Parasitol. Res., 2001, 87, p449-452, cited in PTO-892).

Castro Hermida et al. disclose the use of β-CD to reduce Cryptosporidium infection in the murine model. See Castro Hermida et al., page 449, abstract. Castro Hermida et al. disclose the pharmaceutical composition of the β-CD in sterile water delivered orally to mice. See Castro Hermida et al., page 450, left column, lines 50-53. The infection is an intestinal tract infection. See Castro Hermida et al., page 450, right column, lines 24-27. The dose administered is 34 mg/kg body weight, administered once daily for the one day of the experiment, and its use in the treatment of disease is suggested. See Castro Hermida et al., page 451, β-CD entry on table 2 and left column, lines 23-30 and right column, lines 16-18.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Ardin Marschel can be reached on 571-272-0718 or Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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